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ORIGINAL RESEARCH

Intravascular Imaging-Guided Versus Coronary Angiography-Guided Complex PCI: A Meta-analysis of Randomized Controlled Trials

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ABSTRACT

Introduction: Trials evaluating the role of intravascular imaging in percutaneous coronary intervention (PCI) for complex coronary artery disease have yielded mixed results. This study aimed to compare the outcomes of intravascular imaging specifically intravascular ultrasound (IVUS) with those from conventional coronary angiography in complex PCI.

Methods: Comprehensive electronic search of MEDLINE, EMBASE, and Cochrane databases was performed until March 2023 for randomized clinical trials (RCTs) comparing intravascular imaging with coronary angiography in patients undergoing complex PCI. Complex PCI was defined per each study, and included PCI for American College of Cardiology/American

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Heart Association (ACC/AHA) type B2/C lesions, unprotected left main coronary artery disease, or multivessel stenting. The primary study outcome was major adverse clinical events (MACE).
Results: The meta-analysis included 10 RCTs with a total of 6615 patients (3576 in the intravascular imaging group and 3039 in the coronary angiography group). The weighted mean-follow up was 28.9 months. Compared with coronary angiography, intravascular imaging reduced MACE (8% vs. 13.3%; relative risk [RR] 0.63; 95% confidence interval [CI] 0.54–0.73), cardiac death (RR 0.47; 95% CI 0.31–0.73), definite/probable stent thrombosis (RR 0.48; 95% CI 0.24–0.97), target vessel revascularization (RR 0.62; 95% CI 0.46–0.83), and target lesion revascularization (RR 0.61; 95% CI 0.47–0.79). There was no difference between both groups in all-cause death (RR 0.79; 95% CI 0.53–1.18) and myocardial infarction (RR 0.80; 95% CI 0.61–1.04).
Conclusion: In patients undergoing complex PCI, intravascular imaging—specifically IVUS—reduced MACE by decreasing the incidence of cardiac death, stent thrombosis, and target vessel and target lesion revascularization.

Keywords: Intravascular imaging; IVUS; Complex PCI; PCI; CA

Key Summary Points

Why carry out this study?
The role of routine use of intravascular imaging in complex percutaneous coronary intervention (PCI) remains unclear.
Our study aimed to compare the outcomes of intravascular imaging (specifically intravascular ultrasound) with conventional coronary angiography in complex percutaneous coronary intervention (PCI).
What was learned from the study?
Complex PCI guided by intravascular imaging reduced the risk of major adverse cardiac events, cardiac death, definite/probable stent thrombosis, and target vessel and target lesion revascularization compared with coronary angiography.
Further efforts should be directed towards identifying the barriers behind the low use of intravascular imaging especially in complex coronary artery interventions.

INTRODUCTION

Despite evolutions in the development of drug-eluting stents (DES) and technical advances in equipment, percutaneous coronary intervention (PCI) for complex coronary anatomy continues to pose a significant challenge. According to the American College of Cardiology/American Heart Association (ACC/AHA) lesion morphology classification, class B2 and C lesions are considered to represent complex anatomy, and include features such as ostial location, extensive calcification, chronic total occlusion (CTO), or long diffuse lesions. Complex PCI, including PCI for patients with complex coronary lesions, unprotected left main (LM) coronary artery disease, or multivessel disease, is associated with worse clinical outcomes due to the high risk of complications and higher rates of target lesion failure [1–7]. Intravascular imaging, using intravascular ultrasound (IVUS) or optical coherence tomography (OCT), was developed to overcome the limitations of conventional coronary angiography [8, 9]. Intravascular imaging enables meticulous assessment of coronary vessels and provides detailed information on the blood vessel wall, coronary plaque, and stent morphological characteristics; thus it enables a patient-tailored approach when managing patients with coronary artery disease (CAD) [10]. Yet, intravascular imaging is still not widely used in real-world clinical practice in part because of lack of experience

in interpreting images, prolonged procedure times, and concerns about reimbursement [9, 11]. The use of intravascular imaging has been recommended by major scientific cardiology societies, to guide and optimize stent implantation in selected cases including complex PCI [12–14]. Several randomized clinical trials (RCTs) have evaluated the role of intravascular imaging compared with coronary angiography for guiding complex PCI [15–24]; however, many studies were underpowered. Therefore, we performed a systematic review and meta-analysis of RCTs comparing the outcomes of intravascular imaging-guided versus coronary angiography-guided complex PCI.

METHODS

Data Sources and Search Strategy

A comprehensive electronic search of MEDLINE, EMBASE, and Cochrane databases was performed through March 2023 for RCTs that compared the safety and efficacy of intravascular imaging with either IVUS or OCT compared with coronary angiography in complex PCI. The following search terms were used: "intravascular imaging" OR "IVUS" OR "coronary angiography" OR "DES" AND "CAD" OR "coronary artery disease". Additional screening of the bibliographies of the retrieved articles, ClinicalTrials.gov, and prior meta-analyses to identify other related studies that did not appear in the initial search. This study was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [25] (Supplemental Table 1) and the details of the systemic review were prospectively registered at PROSPERO (ID 411453).

Selection Criteria

This study included RCTs that evaluated the safety and efficacy of intravascular imaging versus coronary angiography in complex PCI. Complex PCI was defined as per each study (Supplemental Table 2). Only studies conducted in human subjects were included and there was no language restriction. Conference abstracts, review articles, case reports, and cohort and non-randomized trials were excluded.

Data Extraction

Data that met the inclusion criteria were extracted by two investigators independently (MH and SM) which included the study features, baseline characteristics, and clinical outcomes. Any discrepancy between investigators was resolved by consensus.

Outcomes

The study's primary outcome was major adverse cardiac events (MACE) as defined by each individual study (Supplemental Table 3). The secondary outcomes included cardiac death, all-cause death, definite/probable stent thrombosis, target vessel revascularization (TVR), target lesion revascularization (TLR), myocardial infarction (MI), post-procedural minimal luminal diameter (MLD), procedural time, and fluoroscopy time. Definite/probable stent thrombosis was defined according to the Academic Research Consortium (ARC) [26, 27]. MI was defined per each study (Supplemental Table 4). Clinical outcomes were reported with the longest follow-up period and on an intention-to-treat basis.

Assessment of Quality of Included Studies

The Cochrane bias risk assessment tool was used to evaluate the quality of the included trials, which included various criteria: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias [28]. Studies were then classified into low risk, high risk, or unclear risk of bias (Supplemental Table 5).

Statistical Analysis

Data were pooled by using random effects model utilizing the Mantel–Haenszel method. I^2 statistic was used to assess the statistical heterogeneity among the included studies. I^2 values of less than 25% were considered low degree of heterogeneity, 25–50% were considered moderate degree of heterogeneity, and greater than 50% were considered a high degree of heterogeneity [29]. Outcomes were reported as risk ratios (RR) for categorical variables and mean differences (MD) for continuous variables. The following sensitivity analyses were conducted: excluding studies with high risk of bias, including studies with consistent MACE definitions, including studies with consistent follow-up at 1- and 2-years outcome, and including studies exclusively using second-generation DES. Subgroup analyses including studies reporting LM coronary artery PCI and CTO PCI were also conducted. *P* values less than 0.05 were considered significant. Publication bias was assessed by using funnel plots. Statistical analyses were conducted using RevMan 5.4 software (Cochrane Collaboration, Oxford, UK).

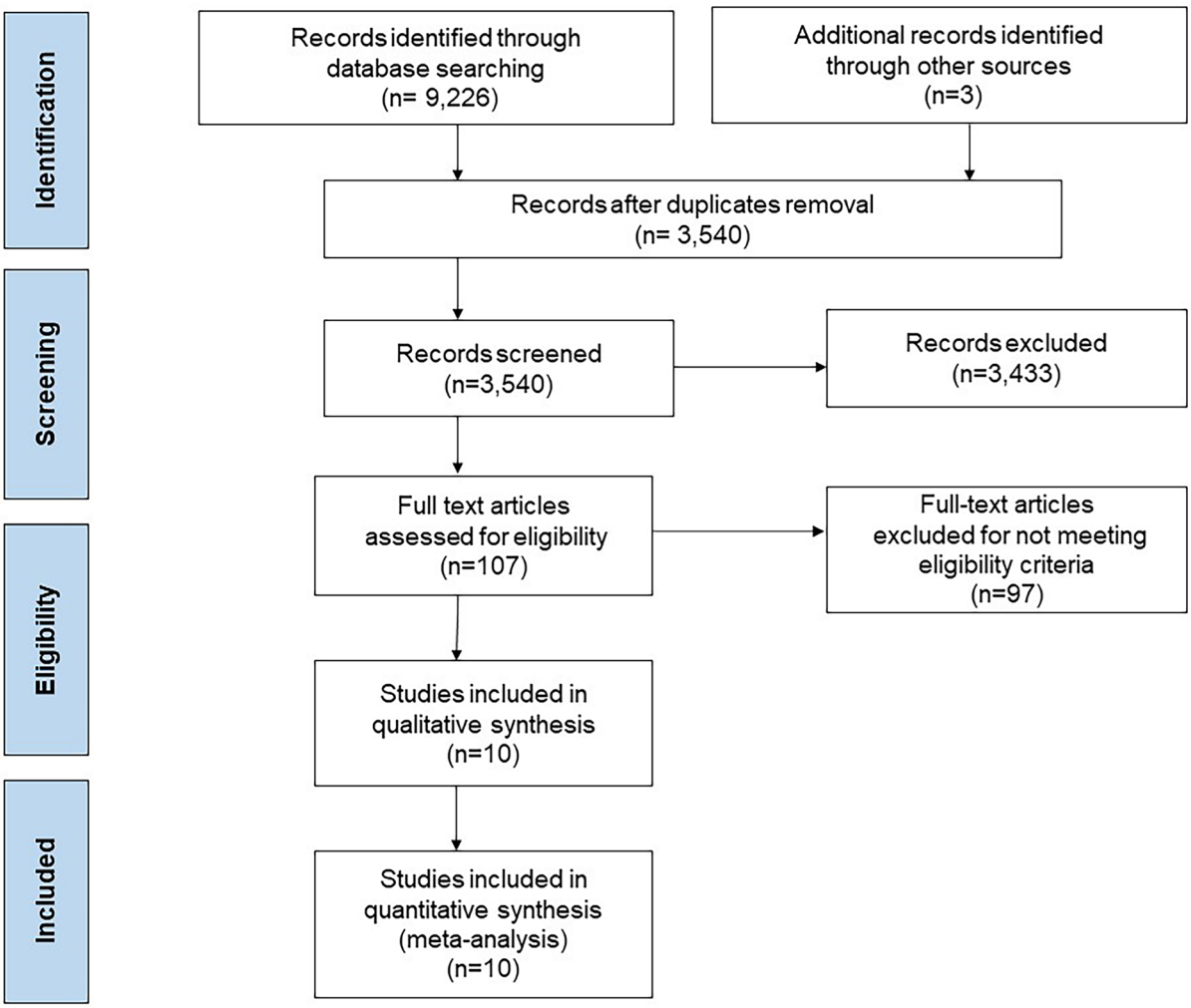


Fig. 1 Study flowsheet

Table 1 Characteristics of the included studies

Study	Year of publication	No. of centers	Country	Group 1 (intravascular imaging-guided)	Group 2 (coronary-guided angiography)	Longest follow-up duration	Inclusion criteria	Primary outcome	Stent type
HOME DES IVUS	2010	Single-center	Czech Republic	105	105	18 months	Complex coronary lesions or complex patient characteristics such as type B_2 and C according to the American Heart Association, proximal left anterior descending artery, left main disease, reference vessel diameter < 2.5 mm, lesion length > 20 mm, in-stent restenosis, insulin-dependent diabetes mellitus, and acute coronary syndrome were included in this study	To assess the role of IVUS guidance during implantation of DES on long-term outcome in patients with high clinical and angiographic	CYPHER (sirolimus-eluting stents) and TAXUS (paclitaxel-eluting stents)
Kim et al. [23]	2013	Multi-center	South Korea	269	274	12 months	Age > 20 years and had a de novo lesion requiring a stent ≥ 28 mm in length in a vessel with a distal reference diameter ≥ 2.5 mm by visual angiographic estimation	MACE	Endeavor Sprint zotarolimus-eluting stents (E-ZES) or everolimus-eluting stent (EES) (Xience V, Abbott Vascular, Santa Clara, California)

Table 1 continued

Study	Year of publication	No. of centers	Country	Group 1 (intravascular imaging-guided)	Group 2 (coronary-guided angiography)	Longest follow-up duration	Inclusion criteria	Primary outcome	Stent type
AVIO	2013	Multi-center	Italy	142	142	24 months	Complex lesions defined as one of the following: long length (> 28 mm); CTO, i.e., a total occlusion of duration more than 3 months; lesions involving a bifurcation; small vessels (≤ 2.5 mm) and patients requiring 4 or more stents	Post-procedure in lesion minimal lumen diameter	DES
AIR-CTO	2015	Multi-center	China	115	115	2 years	Patients aged 18–80 years, who had at least one CTO lesion (defined as TIMI grade 0 and occlusion duration > 3 months) that had been successfully recanalized (defined as a wire-crossed CTO lesion and at the distal true lumen according to angiograms)	In-stent late lumen loss at 1-year follow-up	Either first- or second-generation DES

Table 1 continued

Study	Year of publication	No. of centers	Country	Group 1 (intravascular imaging-guided)	Group 2 (coronary-guided angiography)	Longest follow-up duration	Inclusion criteria	Primary outcome	Stent type
Tan et al. [22]	2015	Single-center	China	61	62	2 years	Unprotected left main coronary artery, defined as at least 50% stenosis by visual assessment in the LM vessel without bypass grafts to the left anterior descending artery or left circumflex artery	MACE	Sirolimus-eluting stents (Firebird-2, Microport, Shanghai, China) or sirolimus-eluting stents (Excel, Jiwei, Shandong, China)
CTO-IVUS	2015	Multi-center	South Korea	201	201	12 months	Patients with CTO who were aged 20–80 years and had typical symptomatic angina or positive test results for functional evaluation of ischemia	Cardiac death	Zotarolimus-eluting stents or Nobori biolimus-eluting stents
Liu et al. [24]	2019	Single-center	China	167	169	12 months	Adults, aged 18–75 years Unprotected left main coronary artery lesions and plan for DES implantation	MACE, defined as cardiac death, MI, or TVR	DES

Table 1 continued

Study	Year of publication	No. of centers	Country	Group 1 (intravascular imaging-guided)	Group 2 (coronary-guided angiography)	Longest follow-up duration	Inclusion criteria	Primary outcome	Stent type
IVUS-XPL	2020	Multi-center	South Korea	700	700	5 years	Patients with typical chest pain or evidence of myocardial ischemia were eligible for enrollment if implantation of an everolimus-eluting stent for a long coronary lesion (implanted stent ≥ 28 mm in length) was indicated on the basis of angiographic lesion length estimation	MACE, defined as cardiac death, target lesion-related MI, or ischemia-driven TLR at 5 years	Everolimus-eluting stent
ULTIMATE	2021	Multi-center	China	724	724	3 years	Patients with silent ischemia, stable or unstable angina, or MI with more than 24 h between onset of chest pain and admission and de novo coronary lesions requiring DES implantation	TVF at 3 years after the index procedure, including cardiac death, target vessel MI, and clinically driven TVR	Second-generation DES

Table 1 continued

Study	Year of publication	No. of centers	Country	Group 1 (intravascular imaging-guided)	Group 2 (coronary-guided angiography)	Longest follow-up duration	Inclusion criteria	Primary outcome	Stent type
RENOVATE-COMPLEX-PCI	2023	Multi-center	South Korea	1092	547	3 years	Patients 19 years of age or older who were undergoing PCI for complex coronary artery lesions, defined as true bifurcation lesions according to the Medina classification system with a side-branch diameter of at least 2.5 mm; a chronic total occlusion; unprotected left main coronary artery disease; long coronary artery lesions that would involve an expected stent length of at least 38 mm; multivessel PCI involving at least two major epicardial coronary arteries being treated at the same time; a lesion that would necessitate the use of multiple stents (at least three planned stents); a lesion involving in-stent restenosis; a severely calcified lesion; or ostial lesions of a major epicardial coronary artery	TVF, defined as the composite of death from cardiac causes, target vessel-related MI, or clinically driven TVR	Polymer-coated everolimus-eluting stents

IVUS intravascular ultrasound, *DES* drug-eluting stent, *CTO* chronic total occlusion, *MI* myocardial infarction, *MACE* major adverse cardiac events, *TLR* target lesion revascularization, *TVF* target vessel failure, *TVR* target vessel revascularization, *PCI* percutaneous coronary intervention, *TIMI* thrombolysis in myocardial infarction, *LM* left main

Table 2 Baseline characteristics of the studies population

Studies	Groups	Age in years, mean (± SD)	Male %	Hypertension %	Diabetes mellitus %	Dyslipidemia %	Current smoking %	Previous PCI %	Previous MI %	Left ventricular ejection fraction %
HOME DES IVUS 2010	Intravascular imaging-guided group	59.4 ± 13	73	67	42	63	40	17	37	–
	Coronary angiography-guided group	60.2 ± 11	71	71	45	66	35	14	32	–
Kim et al. [23]	Intravascular imaging-guided group	62.8 ± 9.3	65.8	61.3	31.6	61.3	21.6	–	1.1	55.3 ± 23.9
	Coronary angiography-guided group	64.3 ± 8.7	54.7	65.8	29.9	61.7	17.2	–	2.9	54 ± 25
AVIO 2013	Intravascular imaging-guided group	63.9 ± 10.1	82.4	70.4	23.9	70.4	34.5	–	–	55.3 ± 8.5
	Coronary angiography-guided group	63.6 ± 11.0	76.8	66.9	26.8	76.8	31	–	–	55.9 ± 8.6
AIR-CTO 2015	Intravascular imaging-guided group	67 ± 10	88.7	74.8	29.6	21.9	39.1	20	20.9	55 ± 11
	Coronary angiography-guided group	66 ± 11	80	70.4	27	27.8	39.1	20.9	30.4	56 ± 12
Tan et al. [22]	Intravascular imaging-guided group	76.54 ± 4.95	62.3	41	34.4	–	44.3	–	16.4	55.32 ± 5.02
	Coronary angiography-guided group	75.85 ± 3.49	69.3	46.8	29.5	–	46.8	–	21	53.33 ± 7.14
CTO-IVUS 2015	Intravascular imaging-guided group	61.0 ± 11.1	80.6	62.7	34.8	–	35.3	15.4	8	56.9 ± 13.1
	Coronary angiography-guided group	61.4 ± 10.1	80.6	63.7	33.8	–	34.3	15.9	8	56.7 ± 11.4

Table 2 continued

Studies	Groups	Age in years, mean (± SD)	Male %	Hypertension %	Diabetes mellitus %	Dyslipidemia %	Current smoking %	Previous PCI %	Previous MI %	Left ventricular ejection fraction %
Liu et al. [24]	Intravascular imaging-guided group	65.3 ± 10.6	63.5	69.5	33.5	37.7	37.1	19.8	17.4	55.6 ± 11.7
	Coronary angiography-guided group	64.9 ± 11.2	63.9	72.2	30.8	37.9	35.5	16.6	14.2	58.4 ± 10.5
IVUS-XPL 2020	Intravascular imaging-guided group	63.0 ± 9.0	69	65	32	68	22	11	5	63 ± 9.8
	Coronary angiography-guided group	64.0 ± 9.0	69	64	36	66	26	10	4	62.3 ± 10.2
ULTIMATE 2021	Intravascular imaging-guided group	65.2 ± 10.9	73.9	70.7	30	53.7	–	–	–	–
	Coronary angiography-guided group	65.9 ± 9.8	73.2	72	31.2	55.2	–	–	–	–
RENOVATE-COMPLEX-PCI 2023	Intravascular imaging-guided group	65.3 ± 10.3	79.6	62.5	36.1	51.3	19.4	24.5	6.9	58.4 ± 11.9
	Coronary angiography-guided group	66.0 ± 10.0	78.8	59	40.8	51.2	17.4	23.2	7.7	59.3 ± 11.0

MI myocardial infarction, *PCI* percutaneous coronary intervention, *SD* standard deviation

Table 3 Baseline quantitative coronary angiographic data of the studies population

Studies	Groups	Coronary artery lesion				Reference vessel diameter (mm) [mean ± SD]	Min luminal diameter (mm) [mean ± SD]	Diameter stenosis % [mean ± SD]	Lesion length (mm) [mean ± SD]
		LAD %	LCX %	RCA %	Left main %				
HOME DES IVUS 2010	Intravascular imaging-guided group	56	–	29	3	3.17 ± 0.43	1.1 ± 0.40	82.3 ± 7.6	18.1 ± 7.3
	Coronary angiography-guided group	54	–	24	4	2.95 ± 0.34	0.97 ± 0.37	79.2 ± 9.3	17.6 ± 6.7
Kim et al. [23]	Intravascular imaging-guided group	62.1	15.2	22.7	–	2.82 (2.58–3.16)[a]	0.95 (0.73–1.23)[a]	–	29.6 (23.2–42.8)[a]
	Coronary angiography-guided group	67.5	12.8	19.7	–	2.80 (2.56–3.15)[a]	0.93 (0.70–1.22)[a]	–	30.6 (24.2–40.9)[a]
AVIO 2013	Intravascular imaging-guided group	53.3	–	–	–	2.67 ± 0.46	0.76 ± 0.46	71.6 ± 15.8	27.4 ± 15.9
	Coronary angiography-guided group	48.6	–	–	–	2.62 ± 0.41	0.65 ± 0.45	75.5 ± 16.1	25.5 ± 15.0
AIR-CTO 2015	Intravascular imaging-guided group	44.3	20.9	34.8	0	Proximal: 2.95 ± 0.37 Distal: 2.26 ± 0.41	–	–	28.48 ± 17.76
	Coronary angiography-guided group	36.5	14.8	46.1	2.6	Proximal: 2.89 ± 0.34 Distal: 2.25 ± 0.44	–	–	29.21 ± 19.11
Tan et al. [22]	Intravascular imaging-guided group	–	–	–	100	–	–	–	–
	Coronary angiography-guided group	–	–	–	100	–	–	–	–

Table 3 continued

Studies	Groups	Coronary artery lesion				Reference vessel diameter (mm) [mean ± SD]	Min luminal diameter (mm) [mean ± SD]	Diameter stenosis % [mean ± SD]	Lesion length (mm) [mean ± SD]
		LAD %	LCX %	RCA %	Left main %				
CTO-IVUS 2015	Intravascular imaging-guided group	41.8	14.4	43.8	–	2.69 ± 0.44	–	–	36.3 ± 17.1
	Coronary angiography-guided group	46.8	15.9	37.3	–	2.64 ± 0.55	–	–	35.5 ± 17.0
Liu et al. [24]	Intravascular imaging-guided group	55.7	44.3	62.3	100	–	–	–	–
	Coronary angiography-guided group	52.7	49.7	58	100	–	–	–	–
IVUS-XPL 2020	Intravascular imaging-guided group	66	13	22	–	2.89 ± 0.46	0.83 ± 0.43	71.2 ± 14.4	34.9 ± 10.8
	Coronary angiography-guided group	60	16	25	–	2.84 ± 0.45	0.82 ± 0.43	71.4 ± 14.4	35.2 ± 10.5
ULTIMATE 2021	Intravascular imaging-guided group	–	–	–	–	–	–	–	–
	Coronary angiography-guided group	–	–	–	–	–	–	–	–
RENOVATE-COMPLEX-PCI 2023	Intravascular imaging-guided group	44.2	19.3	27.4	10.1	Proximal: 3.2 ± 0.5 Distal: 2.7 ± 0.5	0.44 ± 0.37	85.4 ± 11.5	28.4 ± 15.9
	Coronary angiography-guided group	43.2	18.5	26.4	9	Proximal: 3.1 ± 0.5 Distal: 2.7 ± 0.4	0.44 ± 0.36	85.2 ± 11.7	26.8 ± 14.8

LAD left anterior descending, *LCX* left circumflex, *RCA* right coronary artery, *SD* standard deviation

[a]Median (interquartile range)

Ethical Approval

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

RESULTS

Included Studies

The detailed study selection process is shown in Fig. 1. The final analysis included 10 RCTs with a total of 6615 patients: 3576 in the intravascular imaging group and 3039 in the coronary angiography group [15–24]. The characteristics of the included studies are outlined in Tables 1 and 2. The baseline coronary angiographic data are shown in Table 3. The weighted mean follow-up was 28.9 months. The weighted mean age was 64.9 years, and 73.3% of the patients were men. Complex PCI was defined per each study (Supplemental Table 2), and included PCI for type B2/C lesions, unprotected LM coronary artery disease, or multivessel stenting. Most included studies included only patients undergoing complex PCI [15–19, 21–24], while ULTIMATE (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in "All-Comers" Coronary Lesions) included patients undergoing both complex and non-complex PCI [20]. HOME DES IVUS, Tan et al., and Liu et al. were single-center studies [15, 22, 24], while all other studies were multicenter [16–21, 23]. The quality of included studies appears in Supplemental Table 5. All of the included studies were open-label [15–24]. The HOME DES IVUS and Tan et al. studies had unclear risk of outcome assessment bias [15, 22]. In addition, Tan et al. had unclear risk of allocation bias [22]. The other studies were considered to be at low risk for bias. Inspection of the funnel plot suggested no evidence of publication bias (Supplemental Fig. 1).

Primary Outcome

The primary outcome was reported in all included studies [15–24]. The definition of MACE was adopted per each study and was reported in Supplemental Table 3 [15–24]. Intravascular imaging reduced MACE compared with coronary angiography (8% vs. 13.3%; RR 0.63; 95% confidence interval [CI] 0.54 – 0.73), with low degree of heterogeneity (I^2 = 0%) (Fig. 2). Sensitivity analyses excluding studies with high risk of bias (RR 0.63; 95% CI 0.54–0.73, I^2 = 0%), excluding studies including OCT (RR 0.63; 95% CI 0.53–0.74, I^2 = 0%), including studies with consistent MACE definition (i.e., composite of cardiac death, MI, or ischemia-driven repeat revascularization) (RR 0.64; 95% CI 0.54–0.74, I^2 = 0%), including studies at 1-year follow-up (RR 0.64; 95% CI 0.47–0.86, I^2 = 0%), including studies at 2-years follow-up (RR 0.71; 95% CI 0.55–0.93, I^2 = 0%), and including studies exclusively using second-generation DES (RR 0.57; 95% CI 0.47–0.70, I^2 = 0%) showed similar results (Supplemental Fig. 2). Subgroup analyses including studies reporting LM coronary artery PCI (RR 0.62; 95% CI 0.50–0.76, I^2 = 0%) and CTO PCI (RR 0.66; 95% CI 0.55–0.79, I^2 = 0%) showed similar results (Supplemental Fig. 4). Other subgroup analyses including patients undergoing IVUS (RR 0.64; 95% CI 0.55–0.74, I^2 = 0%) and OCT (RR 0.49; 95% CI 0.28–0.85, I^2 = 0%) showed similar results (Supplemental Fig. 4).

Secondary Outcomes

Compared with coronary angiography, intravascular imaging reduced the incidence of cardiac death (1.2% vs. 2.4%, RR 0.47; 95% CI 0.31–0.73; I^2 = 0%), definite/probable stent thrombosis (0.4 vs. 1.2, RR 0.48; 95% CI 0.24–0.97; I^2 = 0%), TVR (4% vs. 7.1%, RR 0.62; 95% CI 0.46–0.83; I^2 = 0%), and TLR (3.6% vs. 6.6%, RR 0.61; 95% CI 0.47–0.79; I^2 = 0%). Intravascular imaging also showed higher post-procedural MLD (MD 0.09; 95% CI 0.05–0.14; I^2 = 62%) compared with angiography. There was no difference between intravascular imaging and coronary angiography groups in all-cause death (3.2% vs. 3.5%, RR 0.79; 95% CI 0.53–1.18; I^2 = 0%) and

MI (3.4% vs. 4.2%, RR 0.80; 95% CI 0.61–1.04; I^2 = 0%). Intravascular imaging required longer procedural time (MD 11.47; 95% CI 6.24–16.70; I^2 = 69%) and fluoroscopy time (MD 4.76; 95% CI 3.49–6.03; I^2 = 0%) (Figs. 2, 3).

DISCUSSION

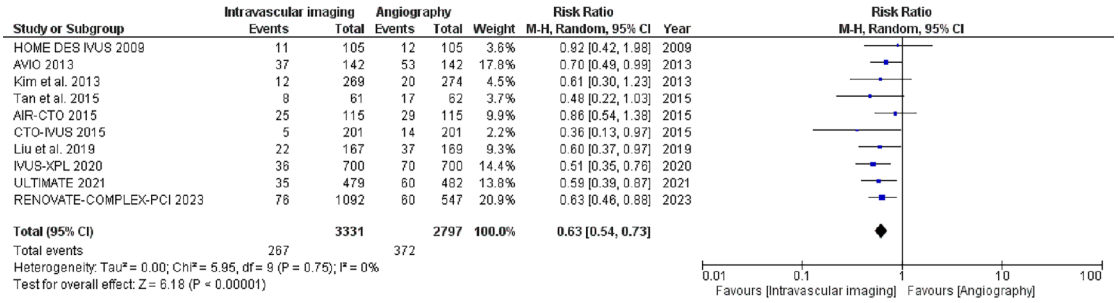
In this meta-analysis of 10 RCTs, including 6615 patients, we evaluated the role of intravascular imaging-guided versus angiography-guided complex PCI. The principal study findings are (1) compared with coronary angiography, complex PCI guided by intravascular imaging was associated with a lower risk of MACE; (2) this benefit was driven by a lower incidence of cardiac death, definite/probable stent thrombosis, and target vessel and target lesion revascularization; (3) there was no difference between angiography- or intravascular imaging-guided complex PCI in all-cause death or MI.

Intravascular imaging-guided PCI was compared with coronary angiography-guided PCI in prior meta-analyses [9, 30–34]. However, the present meta-analysis is the only one focusing on complex PCI. Prior individual RCTs have shown that the use of intravascular imaging was associated with a reduction of MACE in complex coronary artery lesions [15–19, 23]. Our analysis not only showed a decreased risk of MACE but also showed reduced risk of cardiac death, TVR, and TLR, and resulted in higher post-procedural MLD. Moreover, this current analysis suggested a numerical reduction in the incidence of MI that did not reach a statistically significant difference. In the current meta-analysis, we included the totality of available RCTs, including the recent RENOVATE-COMPLEX-PCI trial. RENOVATE-COMPLEX-PCI involved 1639 patients with a median follow-up of 2.1 years; it demonstrated that intravascular-guided imaging showed a lower risk of a composite of cardiac death, target vessel-related MI, or TVR/TLR that was consistent with prior study results. Moreover, RENOVATE-COMPLEX-PCI is the only study that included either IVUS or OCT for intravascular-guided imaging, while other studies used only IVUS [21].

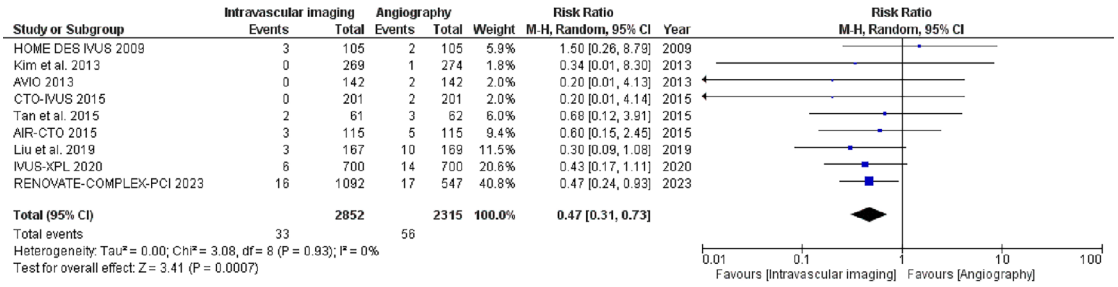
Complex coronary artery lesions are challenging to manage and necessitate careful consideration of the best treatment strategy. Coronary angiography has some drawbacks as it provides only a 2-dimensional view of the complex 3-dimensional coronary artery lumen. It also lacks a detailed understanding of plaque morphology and vessel size [32]. There are different intravascular imaging modalities, including IVUS and OCT which are the most common and widely used intravascular imaging techniques. OCT can provide higher spatial resolution with better tissue characterization, while IVUS allows better tissue penetration that enables full-thickness visualization with lower resolution which helps the operator with decision-making in the PCI optimization [35, 36]. Both intravascular imaging techniques are complementary tools and the use of one of these tools depends on the individual's expertise [37]. In addition, previous studies have shown that OCT was noninferior to IVUS [38]. The mechanism of intravascular imaging to improve outcomes is related to multiple factors. Intravascular imaging can provide a high-resolution cross-sectional image with detailed tomographic structural information of the anatomy of the coronary artery, such as plaque morphology and vessel size [9]. Furthermore, intravascular imaging encourages optimal coronary stent sizing while avoiding stent malposition and underexpansion [39, 40]. Moreover, it allows for the detection of complications such as edge dissections that may be missed with coronary angiography [41]. The use of intravascular imaging in calcific lesions is essential to assess the lesion morphology, as it can help quantify the calcium distribution and determine the need for atherectomy [42–44]. Intravascular imaging may also improve the safety and efficacy of atherectomy for calcific lesions [42–44]. The role of intravascular imaging use in LM coronary interventions has been robustly established, allowing assessment of disease distribution and plaque morphology that may help guide decisions around the need for an upfront two- versus one-stent approach [45, 46].

The inconsistent use of intravascular imaging amongst operators in routine clinical

Major adverse cardiac events (MACE)

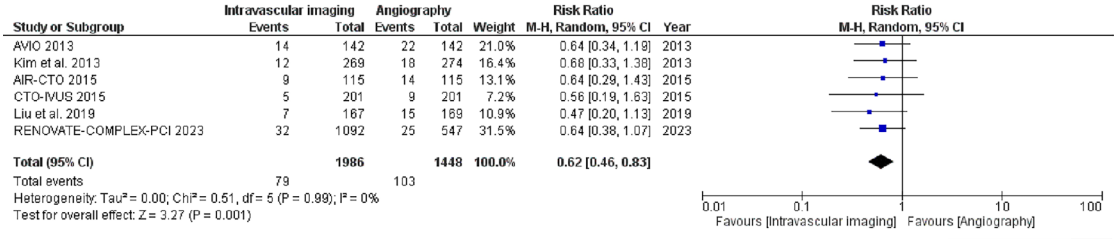


Cardiac death

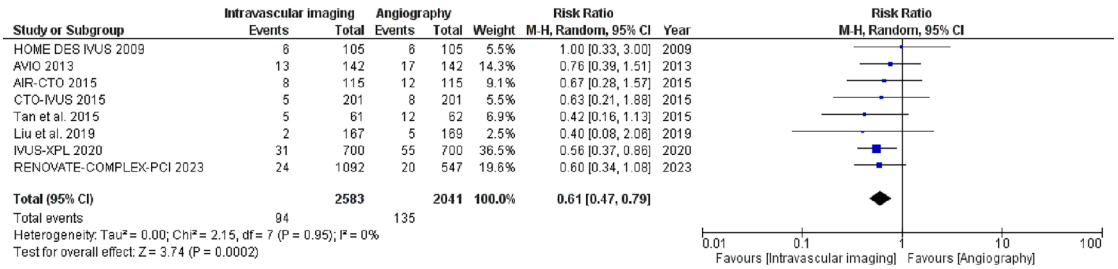


Definite/probable stent thrombosis

Target vessel revascularization (TVR)



Target lesion revascularization (TLR)



◂**Fig. 2** Forest plot for MACE, cardiac death, definite/probable stent thrombosis, target vessel revascularization, and target lesion revascularization among intravascular imaging versus coronary angiography groups. *CI* confidence interval, *M–H* Mantel–Haenszel

practice may be related to increased procedural time, operator experience, and concerns of higher costs related to intravascular imaging when compared with coronary angiography [47]. However, intravascular imaging has

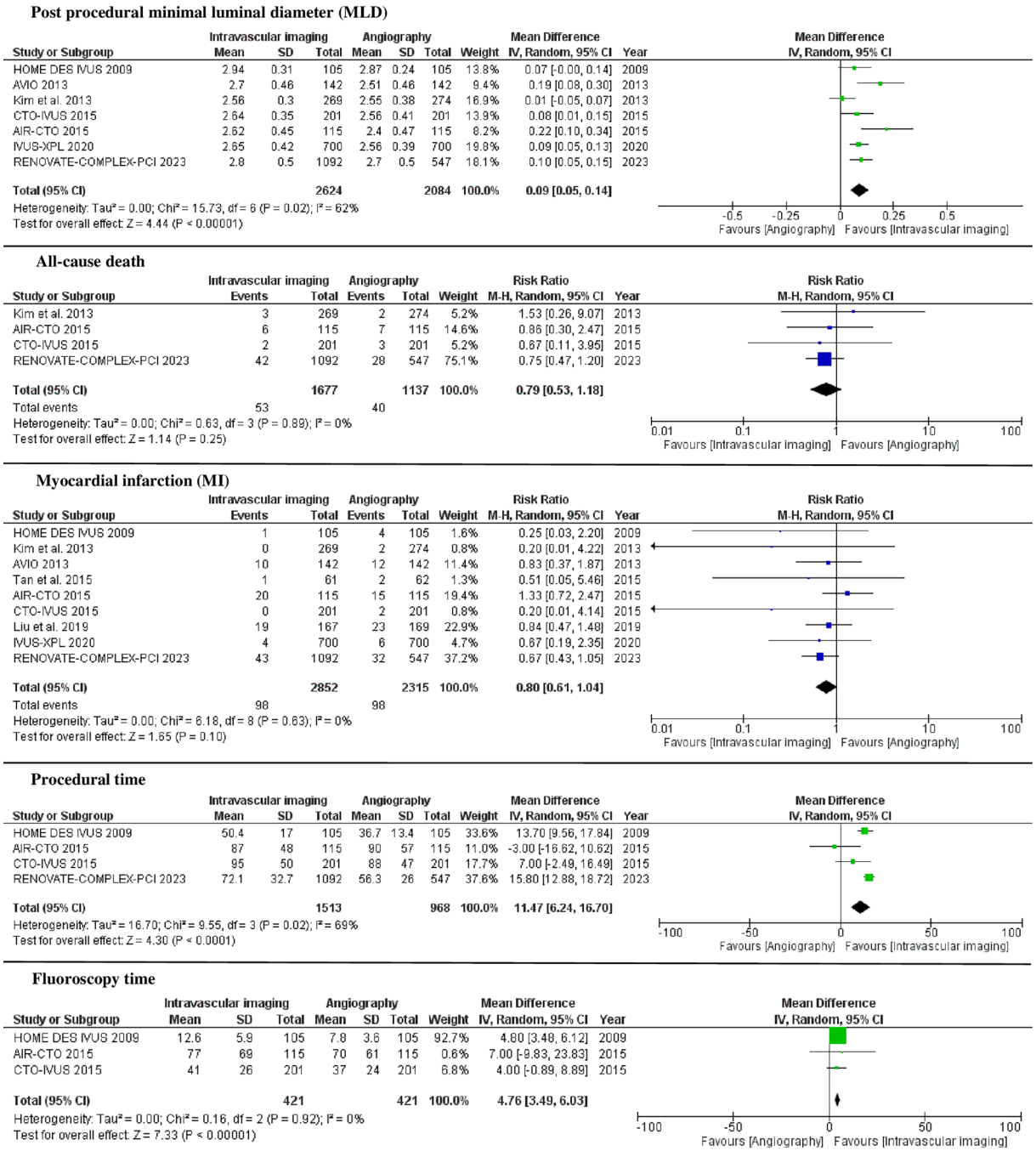


Fig. 3 Forest plot for post-procedural minimal luminal diameter, all-cause death, MI, procedural time, and fluoroscopy time among intravascular imaging versus coronary angiography groups. *CI* confidence interval, *IV* inverse variance, *M–H* Mantel–Haenszel

proven overall cost-effectiveness as it improves the overall burden on healthcare system by lowering costs for hospitalizations and urgent TVR [48, 49].

Our study had few limitations. First, studies included in the current analysis included various forms of complex coronary lesions and we could not ascertain outcome per types of complex lesions. Second, the use of OCT was evaluated only in one study, which might limit the generalizability of the study results to OCT. Third, the included studies used various types of DES which could alter the study outcomes, so we conducted a sensitivity analysis including studies exclusively using second-generation DES. Fourth, the mean follow-up time was 28.9 months; longer follow-up could alter the observed outcomes. Fifth, there was a lack of patient-level data that prohibited more granular analyses.

CONCLUSIONS

Among patients undergoing complex PCI, intracoronary imaging guidance reduced the risk of MACE compared with angiography guidance, an effect that was driven by reducing the incidence of cardiac death, definite/probable stent thrombosis, and target vessel and target lesion revascularization. Further efforts should be directed towards identifying the barriers behind the low use of intravascular imaging especially in complex coronary artery interventions.

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Declarations

Conflict of Interest. Mohamed Hamed, Sheref Mohamed, Mohamed Mahmoud, Jonathan Kahan, Amr Mohsen, Faisal Rahman, Waleed Kayani, Fernando Alfonso, Emmanuel S. Brilakis, Islam Y. Elgendy, Mamas A. Mamas, and Ayman Elbadawi have nothing to disclose.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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